AMENDMENTS TO THE DRAWINGS:

The attached four sheets of drawings include changes to Figures 1-4. These sheets replace the original four sheets including Figures 1-4.

Attachment: 4 Replacement Sheets

REMARKS

This application is amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claim 20 is amended. Support for the amendment to claim 20 may be found generally throughout the specification, e.g., page 5, lines 23-28, page 6, lines 7-20, and page 9, lines 13-22.

Claims 20-38 remain pending in the application, with claims 26-38 being withdrawn for being directed to a non-elected invention.

The present specification is amended to include section headings, including a Description of the Drawings. Support for the Description of the Drawings is as follows:

Figure 1: page 19, lines 22-26 and page 20, lines 9-12.

Figure 2: page 20, lines 20-23.

Figure 3: page 26, lines 3-6.

Figure 4: page 27, lines 27-30.

The Official Action objects to the specification for including various informalities. This objection is traversed.

The informalities are discussed below, with reference to their designated item number from the Official Action:

I. Items 1 and 6, i.e., the Luminex® particles/sensitized particles/colored polystyrene particles.

The Official Action believes that these terms are indefinite and unclear. However, the present specification and claims describe the particles utilized in the present invention in terms of their function, their composition, and their size. For example, the general description of the particles, including the possible polymers from which they are made, is provided at page 4, line 28, to page 5, line 13. Additionally, the meaning of "sensitized" particles is described at page 5, line 35 to page 6, line 4, in general terms. Sensitized particles are described in more specific terms at page 6, line 36, to page 7, line 17.

The system of sensitized particles, e.g., colored polystyrene particles, used in the examples belong to the Luminex® system of sensitized particles, as disclosed at page 17, line 36, to page 18, line 12. In the examples, the specific particle size, particle composition, and the groups with which the particles are functionalized, i.e., sensitized, are described.

Thus, the physical characteristics of the particles required to carry out the claimed invention are described in a definite manner throughout the present specification.

II. Items 2 and 3, i.e., the flow cytometer and first laser.

The Official Action states that these terms are indefinite because the specific manufacturer and model number, for example, are not disclosed. However, the claimed invention is directed to a method for preparing an immunoreagent which goes into making of a calibration system. The method is not limited to the particular manufacture or model number of the equipment that may be used to carry out the claimed invention.

It is not necessary that every last detail of an invention be described, by working examples or otherwise. *Ex parte Wolters et al.* (POBA 1979 214 USPQ 735). The patent specification is not intended to be a production specification. *In re Gay* (CCPA 1962) 309 F.2d 768, 135 USPQ 311.

Indeed, the present specification describes a technique for quantifying analytes using flow cytometry that was previously described in the publications WO 99/36564 and WO 97/14028, as disclosed at page 1, line 35 to page 2, line 15 of the present specification.

III. Items 4 and 5, i.e., the "external fluorescent compound".

The external fluorescent compound is a compound having excitation and admission wavelengths different from those of the particles including analyte-ligand reactions. See, e.g., the paragraph bridging pages 4 and 5 and the first paragraph of page 18. The purpose of the external compounds is for quantifying the

analyte-ligand reaction particles. Thus, the present specification describes the external fluorescent compound in a definite manner to enable one to carry out the disclosed invention.

IV. Item 7 and 17, i.e., the phrases "as described above" and "as indicated above", respectively.

The present specification discloses in the paragraph bridging pages 18 and 19, that "the amounts of each ligand, or antigen, which had to be attached to the various categories of particles were determined according to the invention, as described above." Accordingly, based on the context, "as described above" refers to, e.g., page 3, line 9 to page 4, line 4, which describes the present invention and the determination of the amounts of a ligand.

In the case of the phrase "as indicated above", it is apparent based on the example that this term refers to the steps preceding the data table, i.e., page 18, line 20, to page 21, line 1.

V. Items 8, 9, and 10, i.e., the "nature of the antigen" and the various terms identifying the antigens.

As to the phrase "nature of antigen", it is apparent from the specification that the table states "nature of the antigen" to describe the column including the various types of

antigens. One of ordinary skill in the art would recognize that the term "nature" in this context does not relate to the realm of philosophy, as stated in the Official Action.

As to the various terms used to identify the antigens, these terms, e.g., SSA and SSB, are well known in the art, and one of ordinary skill in the art upon reading the present specification would readily understand which antigens are identified in the present specification.

VI. Items 11, 12, and 14-16, directed to the disclosed concentration of "micrograms".

The Official Action refers to concentrations disclosed in the two paragraphs between lines 9 and 29 of page 20. However, the first sentence of each paragraph discloses that the concentration units are expressed in micrograms per ml of particles. Indeed, the subsequent sentences refer back to these concentrations described in the first sentence. Thus, one of ordinary skill in the art would recognize that the concentrations described in the subsequent sentences referred to micrograms per ml of particles.

VII. Item 13, i.e., "the antigen antibody reaction".

The Official Action states that this phrase lacks antecedent basis. However, this phrase is described generally throughout the specification, as the general description of the

technique, e.g., at page 2, lines 7-10 and the paragraph bridging pages 4 and 5. Thus, the phrase is understood in the context of the present specification.

Therefore, in view of the above, the specification is definite, and withdrawal of the rejection is respectfully requested.

The Official Action objects to the drawings because the drawings are missing axes labels.

Corrected drawings including axes labels are included with this amendment.

Therefore, withdrawal of the objection to the drawings is respectfully requested.

Claims 20-25 are rejected under 35 USC §101 for allegedly lacking patentable utility. This rejection is respectfully traversed.

The Official Action alleges that the utility asserted in the present application is not credible. However, the Official Action fails to establish a *prima facie* case and provide evidentiary support of the alleged lack of utility. See, e.g., MPEP §2107.02 IV. Indeed, the Official Action fails to provide an evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

The Official Action further asserts that the present application discloses a hypothetical range with "pretend, imaginary" biological units.

However, with respect to the alleged lack of utility and especially the "pretend, imaginary" units of measure, an aspect of the present invention relates to a calibration method requiring a single calibration system only, for simultaneously quantifying several analytes in the same biological sample.

The first step of this method includes determining the curve of response as a function of the concentration of homologous compound, as defined on page 5, lines 23-28, over a range of concentrations corresponding to the known measurement range of each analyte to be assayed.

The known measurement range of each analyte is expressed in International Units when possible. However, this is not always the case.

The examples of the present invention concern simultaneous assaying of:

- the ANA directed against the antigens of SSA, SSB, Sm, Sm/NRP, Scl70, Jo1, dsDNA and centromere; and

- the ANCA directed against the antigens of MPO and PR3.

Standard reagents, recognized by the World Health Organization and enabling the expression of quantitative results in International Units, exist only for antibodies directed against the antigen of dsDNA.

For the other analytes quoted in the examples, i.e., SSA, SSB, Sm, Sm/NRP, Scl70, Jo1, centromere, MPO and PR3, no

system of International Units recognized by the World Health Organization exist.

For this reason, the Applicant used, as standards, samples which are characterized and certified with respect to clinical biological criteria.

For example, for antibodies directed against the antigens of SSa, SSB, Sm, NRP, Scl70, Jo1 and centromere, reference reagents are made available by the Arthritis Foundation and the Centers for Disease Control in the USA (please refer to the enclosed pages from the website springerlink.com in the Appendix of this amendment).

These reference reagents allow the detection of these antibodies and thus, are positive controls for the Applicant's assays.

Thus, quantitative results obtained according to the present invention are expressed in Biological Units, which are typically standard units of expression of presence or absence of ANA and ANCA in biological samples.

Therefore, for the reasons stated above, the asserted utility is credible and withdrawal of the rejection is respectfully requested.

Claims 20-25 are rejected under 35 USC §112, first paragraph. This rejection is respectfully traversed.

The position of the Official action is that the claimed invention is not supported by either of credibly asserted utility

or a well-established utility, based on the opinions of the Official Action.

However, the initial burden is on the Office to establish a *prima facie* case and provide evidentiary support thereof. As the Official Action fails to provide any support or evaluation of the closest prior art to substantiate the lack of utility conclusion, the Official Action fails to establish a *prima facie* case rejection for lack of utility.

Moreover, as discussed relative to the rejection made under 35 USC §101, the claimed invention does have utility.

Therefore, withdrawal of the rejection is respectfully requested.

Claims 20-25 are rejected under 35 USC §112, second paragraph, as being indefinite. This rejection is respectfully traversed.

The Official Action objects to the transition phrases, the phrase "homologous compound", and the phrase "the known measurement range of the analyte".

The present amendment includes a new transition phrase, i.e., comprising. The "homologous compound" is clarified, i.e., as disclosed at page 5, lines 23-28, and the phrase "the known measurement range" has been clarified in a manner consistent with page 6, lines 7-20 and page 9, lines 13-22. Thus, the claims are believed to be definite.

Therefore, withdrawal of the rejection is respectfully requested.

As no prior art rejections are made in the outstanding Official Action, and the application is amended, applicants believe that the present application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

Robert Madsen, Reg. No. 58,543
745 South 23rd Street
Arlington, VA 22202
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

RM/mjr

APPENDIX:

The Appendix includes the following item(s):

- Four Replacement Sheets for Figures 1-4 of the drawings
- SpringerLink article

Article de revue

Standards for ANA and anti-DNA

Revue	Clinical Rheumatology
Éditeur	Springer London
ISSN	0770-3198 (Print) 1434-9949 (Online)
Numéro	Volume 9, Supplement 1 / mars 1990
DOI	10.1007/BF02205554
Pages	74-81
Subject Collection	Medicine
SpringerLink Date	lundi 10 octobre 2005

T. E. W. Feltkamp[1]

(1) Department of Autoimmune Diseases of the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, P.O. Box 9190, 1006 AD Amsterdam, The Netherlands

Summary *A review of the history, production, characterics and availability of the standards and reference preparations in the field of ANA determination is given. For ANA of the homogeneous type and for anti-DNA standard reagents are recognized by the WHO. This enables the expression of quantitative results in international units, leading to a decrease of interlaboratory variations. For the other types of nuclear fluorescence and for anti-Sm, anti-Ro (SS-A), anti-La (SS-B), anti-Scl 70 and anti-Jo-1, reference reagents are made available by the Arthritis Foundation (AF) and the Centers for Disease Control (CDC) in the USA. For anti-nRNP, a WHO reference reagent exists. The use of the above materials is*

advocated. Requests for WHO standards should be directed to: Dept. of Reagents CLB, P. O. Box 9190, 1006 AD Amsterdam, The Netherlands, and for AF/CDC reagents to: AF/CDC ANA Ref. Lab., Immunology 1 - 1202 A 25, CDC, Atlanta GA 30333, USA.

Key words Standardization - Antinuclear Antibodies - Anti-DNA - Reference Preparation - Immunofluorescence Technique - WHO

References secured to subscribers.

1 article plus récent

1. Nakamura, Robert M. (1994) Current status of available standards for quality improvement of assays for detection of autoantibodies to nuclear and intracellular antigens. *Journal of Clinical Laboratory Analysis* 8(6) [CrossRef]